ening. Liver function tests should be done when this medication is prescribed and, whenever chronic prophylaxis is undertaken, blood levels should be monitored and drug concentrations kept within therapeutic range. Diphenylhydantoin therapy does not prevent recurrence in children younger than 3 years, and intermittent medication is of no benefit. There is no consensus about how long to continue treatment, some authors suggesting until 4 years of age or after one seizure-free year, whichever is later. Parent education both about the nature of the illness and possible side effects of medication is the most important factor in maintaining compliance.

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The Role of Valproic Acid in the Management of Seizure Disorders

VALPROIC ACID (Depakene) was approved for use in the United States as an anticonvulsant in 1978. Subsequent experience with this medication indicates that it is a useful therapeutic agent for several types of seizures but also has significant toxicity.

Valproic acid appears to be more effective for treating generalized than focal types of epilepsy. In several large series, between 50 percent and 75 percent of patients taking this medication had at least 75 percent improvement in seizure control. Patients who have petit mal epilepsy (absence seizures) respond best to valproic acid, though patients who have atypical absence, myoclonic and generalized tonic-clonic seizures also respond well. Infantile spasms and akinetic seizure disorders are minimally affected by valproic acid.

Although it has significant side effects, valproic acid is a useful anticonvulsant medication, especially in refractory cases of generalized seizure disorders. The initial dosage is usually 250 mg four times a day in adults and 15 to 20 mg per kg of body weight a day in children, after which the dosage is adjusted to achieve a blood level of 50 to 100 μg per ml. Valproic acid has a relatively short half-life (6 to 15 hours) and is thus given in several doses a day. Some centers, however, have reported improved seizure control with once or twice a day administration. Valproic acid administration increases serum concentrations of phenobarbital and decreases phenytoin concentrations, so that blood concentrations of these medications should be monitored closely when used in combination with this drug. Complete blood counts, platelet counts and liver function tests (determining ammonia content may be especially helpful) should be checked at about two- to three-month intervals while a patient is taking valproic acid.

Despite initial reports of low toxicity, several major adverse effects have been described. At least 50 reports of fatal hepatic necrosis have appeared in this country since 1978. In these cases there does not appear to be a clear relationship between the hepatic disorder and dosage, duration of time taking valproic acid or serum aspartate aminotransferase values. Withdrawal of the drug after symptoms appear has not always led to reversal of the problem, and some patients have later died of liver disease despite drug withdrawal early in the course. Acute pancreatitis, in at least one instance, has also been reported to occur in association with valproic acid use. Less dangerous side effects include gastrointestinal disturbances (nausea, vomiting, diarrhea and changes in appetite), which occur in as many as 45 percent of patients. Alopecia (usually mild) has been found in 0.5 percent to 4 percent of patients. Valproic acid inhibits the second phase of platelet aggregation and may produce clotting abnormalities. Thrombocytopenia has also been reported rarely.

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Gilles de la Tourette's Syndrome

GILLES DE LA TOURETTE'S SYNDROME (GTS) is a disorder consisting of multiple motor tics and vocalizations, which begins in childhood or early adolescence. Coprolalia, the involuntary utterance of obscenities, long considered to be pathognomonic, is present in less than half of patients. Related features such as echolalia, palilalia and compulsive behaviors are not always present but help to clarify the diagnosis when they are. The clinical course characteristically waxes and wanes.

The lack of neuropathological findings in GTS

has led to an array of psychological explanations of the unusual characteristics. Shapiro and associates established GTS as a neurologic disorder with an increased incidence of sinistrality, generalized electroencephalographic abnormalities, neurological soft signs and organic indices found on psychological testing. The response of the tics to haloperidol suggested that GTS is a disorder of central dopaminergic activity. With the introduction of clonidine (a presynaptic α_2-noradrenergic agonist) for the treatment of GTS (Cohen and coworkers 1980), an alternative pharmacologic approach became available that focused attention on noradrenergic systems.

Behavioral features including hyperactivity, impulsivity, compulsivity, irritability and a low frustration tolerance have recently been emphasized. Shapiro and colleagues reported that more than half of their GTS cases met criteria for a diagnosis of hyperkinetic syndrome (minimal brain disturbance, now called attention-deficit disorder). Other features such as obsessive-compulsive behavior are less universally accepted but appear to be increasingly prevalent in GTS.

Clonidine may most beneficially affect the behavioral abnormalities, whereas haloperidol affects the tics. Because of the overall lower incidence of significant side effects, clonidine has been useful in treating patients who are unresponsive to or who cannot tolerate the side effects of haloperidol. A combination of the two drugs often produces beneficial effects, even when both drugs are given in lower doses than is useful if either is given alone. Experimental treatments using drugs that exert their primary effects on cholinergic and γ-aminobutyric acid-aminergic systems have met with limited success.

Two new syndromes related to GTS have been described. *Toxic Tourette's syndrome* is the development of GTS in children treated with stimulant medications for hyperkinetic syndromes. It is unclear whether these medications cause expression of an underlying predisposition toward the development of GTS. Because the syndrome is irreversible in some patients, even when the medications are withdrawn, caution is advised in the use of these agents.

Tardive Tourette's syndrome describes the development of a GTS-like disorder in patients exposed to high doses of neuroleptic medication for several years. Most patients with this syndrome have been schizophrenic.

Gilles de la Tourette's syndrome should be viewed as a "pervasive neuropsychiatric" syndrome with motor and behavioral features, both of which should be considered in the evaluation and treatment of the disorder.

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Neurologic Complications of Routine Immunization

COMPLICATIONS FOLLOWING IMMUNIZATION have been described at each anatomic level of the nervous system: peripheral nerve, nerve root and nerve plexus, spinal cord and brain. Awareness of these complications will aid a physician in the diagnosis and treatment of many unexplained acute neurologic problems following immunization.

A disorder of distal peripheral nerves resembling carpal tunnel syndrome has been described following rubella immunization. Clinically patients have intense pain at the wrist (and sometimes the knee), occasionally bilaterally, with pain most severe at night. Latency of onset is 10 to 70 days, with a mean of 45 days, after immunization. Electrophysiologic studies show slowed median nerve conduction velocity and prolonged median nerve motor and sensory distal latency. This syndrome resolves completely without any specific therapy usually within a month.

Brachial plexopathy has occurred following immunization. Peak incidence of occurrence is usually two to three weeks after immunization. Administration of tetanus toxoid or horse tetanus antitoxin is occasionally asssociated with this complication. This syndrome is often heralded by intense pain in the shoulder, arm and hand, but most patients recover completely. Treatment with steroids has not been provèd effective.

Guillain-Barré syndrome has been linked epidemiologically to the A/New Jersey (swine flu) National Influenza Immunization Program of 1976. The peak period of increased risk was within five weeks of immunization, and lasted for up to ten weeks. Subsequent influenza immunization programs have not been associated with increased risk of Guillain-Barré syndrome.

The spinal cord is sometimes involved follow-